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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER
EINSMANN, JULIET CAROLINE

ART UNIT	PAPER NUMBER
1634	

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34

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	08/956,991	KORENBERG, JULIE R.	
	Examiner	Art Unit	
	Juliet C Einsmann	1634	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *04 November 2002* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1, 11, 13-19, 21-29 and 31-49* is/are pending in the application.

4a) Of the above claim(s) *11,13-19 and 21-29* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1 and 31-49* is/are rejected.

7)☒ Claim(s) *47 and 48* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *04 November 2002* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

RESPONSE TO APPLICANT'S AMENDMENT

1. The Examiner of your application in the PTO has changed. To aid in correlating any papers for this application, all further correspondence regarding this application should be directed to Juliet Einsmann, Art Unit 1634, Technology Center 1600.

2. Applicant's amendment, filed 11/4/02 (Paper No. 32), is acknowledged. Claims 32, 33, 34, 35, 38, 40, 41, 43, and 44 have been amended. Claims 2-10, 12, 20 and 30 have been cancelled previously. Claims 1, 11, 13-19, 21-29 and 31-49 are pending. Claims 11, 13-19 and 21-29 stand withdrawn from further consideration by the Examiner, 37 C.F.R. § 1.142(b) as being drawn to a nonelected invention. *Claims* 1 and 31-49 *are under consideration in the instant application.*

3. In this Office Action, the status of the previous grounds of rejection is addressed, and then new grounds of rejection are set forth. Arguments set forth with regard to any particular grounds of rejection are The indicated allowability of claims 1, 31, 32, and 45 is withdrawn in view of the New Grounds of Rejection set forth herein.

4. The new drawings received 11/4/02 are approved for examination.

Claim Objections

5. Claims 47 and 48 are objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. Applicant is required to cancel the claim, or amend the claim to place the claim in proper dependent form, or rewrite the claim in independent form.

It is noted that instant claims 33, 34, 35 and 38, from which claims 47 and 48 depend, already limit the nucleic acid to a "complementary DNA." Thus, claims 47 and 48 do not properly limit independent claims 33, 34, 35 and 38.

Applicant argued that although the nucleic acids of claims 33, 34, 35, and 38 comprise the nucleotide sequences of complementary DNAs, they are not necessarily complementary DNA and could include RNA. However, this is not persuasive, because the claims specifically set forth that the claimed nucleic acids comprise the sequence of "complementary DNA." The nucleotide sequence of "complementary DNA" is made up of deoxyribonucleotides, and by definition cannot be RNA which is made up of ribonucleotides. Thus, claim 47 is newly objected to because the limitation of the dependent claims is not within the scope of independent claims 33, 34, 35, and 28. In order to overcome this objection with respect to claim 47, applicant is requested to give an example of a nucleic acid that falls within the scope of one of the independent claims that is structurally distinct from a cDNA molecule.

Claim Rejections - 35 USC § 112

6. The following is a quotation of the second paragraph of 35 U.S.C. 112.
The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

7. Claim 48 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

A) The previous rejection of claims 32, 40 and 43 is withdrawn in light of applicant's amendments to the claims.

B) Claim 48 recites the limitation "the isolated nucleic acid ....which is RNA" and depends from claims 33, 34, 35 and 38 (in addition to claims 1 and 41). There is insufficient antecedent basis for this limitation in the claim with respect to claims 33-35 and 38, because claims 33-35 and 38 limit the nucleic acid to a cDNA. It is suggested that Applicant delete the reference to claims 33-35 and 38 from claim 48.

Applicant argued that although the nucleic acids of claims 33, 34, 35, and 38 comprise the nucleotide sequences of complementary DNAs, they are not necessarily complementary DNA and could include RNA. However, this is not persuasive, because the claims specifically set forth that the claimed nucleic acids comprise the sequence of "complementary DNA." The nucleotide sequence of "complementary DNA" is made up of deoxyribonucleotides, and by definition cannot be RNA which is made up of ribonucleotides.

8. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

9. The previous rejection of claims 33, 34, 36, 37, 47 and 48 under 35 USC 112, first paragraph is withdrawn in view of Applicant's amendment to the claims and arguments, filed 1/25/02.

10. The New Matter rejection of claims 34, 36-43 and 47-49 is withdrawn in view of applicant's amendments which removed the new matter.

11. Claims 33-49 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one

skilled in the relevant art that the inventor, at the time the application was filed, had possession of the claimed invention.

12. This rejection is reiterated from the previous office action and newly applied to claim 45. The rejection has been modified to address newly added limitations to amended claims. The following *written description* rejection is set forth herein.

The Guidelines for the Examination of Patent Applications Under the 35 U.S.C. 112, ¶ 1 "Written Description" Requirement make clear that the written description requirement for a claimed genus may be satisfied through sufficient description of a representative number of species by actual reduction to practice, reduction to drawings, or by disclosure of relevant, identifying characteristics, i.e., structure or other physical and or chemical properties, by functional characteristics coupled with a known or disclosed correlation between function and structure, or by a combination of such identifying characteristics, sufficient to show the applicant was in possession of the genus (Federal Register, Vol. 66, No. 4, pages 1099-1111, Friday January 5, 2001, see especially page 1106 3rd column).

Instant claims 33-35 (and dependent claims 36-37 and 47-49) are each drawn to a genus of nucleic acids which "hybridizes under high stringency conditions" to "substantially the entire complement" various other nucleic acids recited in the claims. For claims 33 and 34, the recited nucleic acids to which the claimed nucleic acids must hybridize smaller portions of full length SEQ ID NO's disclosed in the specification. For claim 35, the recited nucleic acids to which the claimed isolated nucleic acid must hybridize is a partial cDNA sequence of the mouse homologue of the instantly disclosed molecule.

Instant claim 38 (and dependent claims 39-40 and 47-49) is drawn to a genus of nucleic acids comprising nucleotide sequences encoding polypeptides comprising various "subsequences of SEQ ID NO:2".

Instant claim 41 (and dependent claims 42-43 and 47-49) is drawn to a genus of nucleic acid molecules comprising either entire sequences disclosed in the specification or portions of sequences disclosed in the specification. It is noted that this is a Markush type claim that recites a variety of sequences. The nucleic acid molecule comprising instant SEQ ID NO: 1 is considered to have adequate written description. The remaining recited fragments do not represent full length cDNAs or include only portions of full length cDNAs and thus encompass a genus that would include splice variants and full length cDNAs.

Instant claim 44 (and dependent claim 46) is drawn to a genus of oligonucleotides *comprising any* 15 nucleotides of SEQ ID NO:7, SEQ ID NO:8 or a nucleic acid encoding SEQ ID NO:11. There is no restriction on the length of the oligonucleotide, thus permitting an extensive number of flanking nucleotides to be present without providing any description of their sequence.

Although the specification discloses that the polypeptides encoded by the nucleic acids of the invention would be expected to function as neural cell adhesion molecules based upon the presence of several Ig-like C2 domains and fibronectin domains and their expression in neural crest cells (e.g., on pages 9-11, 43-44 and 56-62); this functional activity is not required of the polypeptides or polypeptide fragments encoded by the nucleic acids recited by the instant claim language.

The possible variations in the structure of the polypeptides encoded by the instantly recited nucleic acids variants is extensive. Hybridization can occur when short stretches of identity are shared between two much larger nucleic acids. Although the claims have been amended to indicate that the claimed molecules hybridize over "substantially the entire complement" to the recited fragments, this language is indefinite and still encompasses situations in which only portions of the fragments hybridize. Similarly, subsequences require shared identity only over some defined (e.g., claims 38 and 44) or undefined (e.g., claim 41) minimal length. In each case additional unidentified sequence may be present, and may in fact be the dominant contributor to the structure of polypeptides encoded by such nucleic acids.

There does not appear to be any requirement that relevant, identifying characteristics of the instant nucleic acids must be shared among members of the genus recited. Neither are there testable functions recited for the polypeptides encoded by these variant nucleic acids sequences to provide some correlation between a particular structure and an associated, testable, function. Even with respect to the oligonucleotides recited, the presence of flanking sequence of undefined length and composition prohibits the at least 15 defined nucleotides from providing an adequate structural basis for the extensive genus of oligonucleotides encompassed by the claim. Thus one of skill in the art would not recognize Applicant to be in possession of the genus of nucleic acids and oligonucleotides encompassed by the instant claims.

Consequently, the claimed invention is not described in such a way as to reasonably convey to one of ordinary skill in the art that the inventor, at the time the application was filed, had possession of the invention. See Regents of the University of California v. Eli Lilly & Co.,

119F3d 1559, 1569, 43 USPQ2d 1398, 1406 (Fed. Cir. 1997). Applicant is also directed to the Guidelines for the Examination of Patent Applications Under the 35 U.S.C. 112, ¶ 1 "Written Description" Requirement, Federal Register, Vol. 66, No. 4, pages 1099-1111, Friday January 5, 2001.

Applicant is invited to point to clear support or specific examples of the claimed invention in the specification as-filed.

Response to Remarks

Applicant argues that contrary to the Examiner's allegation that members of the claimed genus lack shared identifying characteristics and testable function, the claimed nucleic acids either hybridize under defined conditions to nucleic acids consisting of a recited sequence or encode a portion of the disclosed DS-CAM protein. However, this argument is not persuasive because the "function" referred to by claims is a function that is more a statement of the structure of the molecule than of some testable function of what the molecule does.

The genus of nucleic acids encompassed by the instant claims includes sequences which are structurally related to the disclosed sequences but which have different activity or biological function. The specification sets forth that the nucleic acids of the instant invention may encode a cell adhesion molecule or may be associated with a variety of neurological disorders. However, the claims encompass within them nucleic acids encoding molecules that are neither of these. For example, claim 33 requires that the claimed nucleic acid hybridize to a portion of the nucleic acid that encodes SEQ ID NO: 11. By requiring that the nucleic acid hybridize to a portion of the nucleic acid encoding SEQ ID NO: 11, but not the entire nucleic acid that encode SEQ ID

NO: 11, the claim encompasses variants of SEQ ID NO: 11 for which no disclosure is provided, such as alternate splice variants. The specification discloses that SEQ ID NO: 11 may be a cell adhesion molecule or may be associated with a variety of neurological disorders. The variants in the claimed genus include molecules that share a common biological activity and thus utility with instant SEQ ID NO: 11, or that do not share such an activity and utility. Yet within this genus, applicant has only described a single set of nucleic acids, that is the set of nucleic acids that encode instant SEQ ID NO: 11. Applicant has not demonstrated possession of other nucleic acids that are alternate splice variant or allelic variants that do not share a common functionality with instant SEQ ID NO: 11. Thus, the claim and those that depend from it remain rejected for lacking adequate written description.

Claim 34 likewise claims nucleic acids that hybridize to nucleic acids that encode two of SEQ ID NO: 2, regardless of the function of the encoded polypeptide. This genus includes any number of possible nucleic acids that encode polypeptides that have separate activity from instant SEQ ID NO: 2. Applicant has only disclosed a single example within this genus, that is the nucleic acid that encodes SEQ ID NO: 2. Applicant has not disclosed a unifying characteristic of the encoded polypeptides that demonstrates possession of the large genus encompassed within the claim. Thus, the claim and those that depend from it remain rejected for lacking adequate written description.

Claim 35 requires that the isolated nucleic acid hybridize to substantially the entire complement of SEQ ID NO: 7 or SEQ ID NO: 8. Claim 41 requires that the claimed isolated nucleic acid comprise SEQ ID NO: 7 or SEQ ID NO: 8 or SEQ ID NO: 9. Each of these is a partial cDNA encoding a portion of a mouse protein. However, these claims encompasses entire

full length sequences, as well as splice and allelic variants which comprise or hybridize to instant SEQ ID NO: 2 and SEQ ID NO: 8 for which no written description is provided in the specification. The fact that the claimed nucleic acids would hybridize to instant SEQ ID NO: 7 and SEQ ID NO: 8 does not in any way appraise the skilled artisan as to the functionality or utility of the encoded polypeptide.

Claims 38, 41, and 44 encompass nucleic acids comprise sequences that encode only portions of the instantly disclosed molecules with any flanking sequences, regardless of the functionality or utility of the encoded polypeptide. Claim 44 requires that the encoded polypeptide have as little as 5 amino acids in common with the disclosed polypeptides. These minimal structural requirements allow for hundreds of thousands of changes to the disclosed sequences while still remaining within the scope of the claims.

Applicant argues that regarding claim 38, one could determine the nucleic acids sequences that encode the portions of SEQ ID NO: 2. The examiner agrees, but the issue with regard to written description is that the claim requires that the claimed nucleic acids comprise a portion that encodes as little as 23 amino acids in common with instant SEQ ID NO: 2, regardless of the functionality of the encoded polypeptide. Amendment of claim 38 to indicate that the claimed nucleic acids CONSIST OF the nucleotide sequence of the encoded polypeptide would overcome the written description rejection.

Applicant argues regarding claim 41 that the claim requires the entire sequences or subsequences recited in the claim, not any portion of them. However, claim 41 still encompasses a number of sequences not adequately described in the claims, including full length mouse sequences and alternate and allelic variants of human and mouse sequences, as previously noted.

Amendment of claim 41 to CONSIST of the recited sequences would overcome the written description rejection.

Claims 44 and 45 requires that the encoded polypeptide have as little as 5 amino acids in common with the disclosed polypeptides, with any flanking sequences. Thus the polypeptides encoded by nucleic acids within the scope of claim 44 include full length mouse sequences and alternate and allelic variants of human and mouse sequences, as previously noted. Amendment of claim 44 to CONSIST of the recited sequences would overcome the written description rejection.

For these reasons and the reasons stated in the rejection, it is concluded that adequate written description does not exist for the claims as broadly drawn, and the rejection is maintained.

18. Claims 33-49 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the nucleic acids consisting of SEQ ID NO:1, SEQ ID NO:10, SEQ ID NOS 7-9, the oligonucleotides consisting of of SEQ ID NOS: 5 and 6, and nucleic acids encoding SEQ ID NO:2 and SEQ ID NO:11; does not reasonably provide enablement for variants of the nucleic acids of SEQ ID NOS:1 and 10 which hybridize, subfragments comprising larger nucleotide sequences or which encode subfragments of the polypeptides of SEQ ID NO:2 or SEQ ID NO:11, or various oligonucleotides of unspecified length and undefined composition. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims.

The specification discloses that the nucleic acids of SEQ ID NO:1 and SEQ ID NO:11 are transcribed in neural crest cells, that the gene responsible for these coding sequences is localized

to a region of chromosome 21 associated with Down Syndrome (21q22.2-22.3), and that the encoded polypeptide is a neural cell adhesion molecule based upon its structural homology with other neural adhesion molecules and its expression pattern (e.g., on pages 9-11, 43-44 and 56-62).

However, as noted supra, the specification does not provide an adequate written description of nucleic acids which hybridize to the various SEQ ID NOS, nucleic acids which are subfragments comprising larger nucleotide sequences of undefined structure and function or which encode subfragments of the polypeptides of SEQ ID NO:2 or SEQ ID NO:11 which are not recited to be associated with any testable function. Consequently, the skilled artisan would not know how to make such nucleic acids.

In addition, the function of polypeptides encoded by these "variant" nucleic acid sequences would be highly unpredictable. The fact that two nucleic acid sequences will hybridize under high stringency conditions does not in and of itself require that the two sequences share any functional activity, nor does the presence of a shared subsequence.

Attwood (Science 2000; 290:471-473) teaches that "[i]t is presumptuous to make functional assignments merely on the basis of some degree of similarity between sequences." Similarly, Skolnick et al. (Trends in Biotech. 2000; 18(1):34-39) teach that even in situations where there is some confidence of a similar overall structure between two proteins, only experimental research can confirm the artisan's best guess as to the function of the structurally related protein (see in particular "Abstract" and Box 2). Finally, even single amino acid differences can result in drastically altered functions between two proteins. For example, Metzler et al. (Nature Structural

Biol. 1997; 4:527-531) show that any of a variety of single amino acid changes can alter or abolish the ability of CTLA4 to interact with its ligands CD80 and CD86 (e.g., summarized in Table 2).

Thus the function of the polypeptides encoded by the instant nucleic acids that hybridize and nucleotide fragments is unpredictable.

Consequently, hybridization language in the absence of *a testable function for the encoded polypeptide* does not allow the skilled artisan to make and use the hybridizing nucleic acids commensurate in scope with the instant claims without undue experimentation.

Similarly, it would require undue experimentation of the skilled artisan to determine which subsequences would have the unrecited function of the full length polypeptide, and in turn identify nucleic acid subsequences which encode these polypeptide subsequences.

Finally, even when the subsequences are derived from a defined sequence, as in instant claim 44, in the absence of direction as to a particular sequence length, it would require undue experimentation of the skilled artisan to select any particular oligonucleotide sequence from a SEQ ID NO: and to further determine what the appropriate flanking sequences should be.

Reasonable correlation must exist between the scope of the claims and scope of enablement set forth. Without sufficient guidance, the changes which can be made in the instantly recited nucleic acid sequences and still encode a polypeptide that maintains the functional properties of the polypeptide of SEQ ID NO:2 or SEQ ID NO:11 is unpredictable, as is the identity of which

subsequences would encode a functional polypeptide; thus the experimentation left to those skilled in the art is unnecessarily, and improperly, extensive and undue.

Response to Remarks

Applicant argues that the claimed nucleic acid molecules are enabled for a use in detecting DS-CAM related molecules. However, the claimed genus of nucleic acid molecules includes hundreds of thousands of nucleic acid molecules that may or may not have some functional relationship to the DS-CAM molecules disclosed herein (as previously discussed in the arguments regarding Written Description). It is highly unpredictable absent further experimentation what the functionality of the nucleic acids encompassed within the claims would be, and it is this lack of unpredictability, in view of the lack of working examples and guidance as to how the instantly disclosed DS-CAM molecules can be modified and retain their functionality that supports the rejection under 112 1st paragraph for lack of enablement.

New Grounds of Rejection

Claim Rejections - 35 USC § 101

13. 35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

14. Claims 1 and 31-49 are rejected under 35 U.S.C. 101 because the claimed invention is not supported by either a specific, substantial and credible asserted utility or a well established utility.

The specification discloses that the nucleic acids of SEQ ID NO:1 and SEQ ID NO:11 are transcribed in neural crest cells, that the gene responsible for these coding sequences is localized to a region of chromosome 21 associated with Down Syndrome (21q22.2-22.3), and that the encoded polypeptide is a neural cell adhesion molecule based upon its structural homology with other neural adhesion molecules and its expression pattern (e.g., on pages 9-11, 43-44 and 56-62). The specification further teaches that SEQ ID NO: 7, SEQ ID NO: 8, and SEQ ID NO: 9 are partial cDNA clones isolated from mice using human DS-CAM cDNA clone as a probe.

The specification asserts that these nucleic acids are useful as probes for assaying for the presence and/or absence of a DS-CAM gene or as probes and primers for amplifying genes encoding DS-CAM proteins (p. 4, lines 5-10). The specification further asserts that the encoded proteins are useful for producing antibodies (p. 4 line 19). A variety of other utilities are asserted, including uses in antisense therapy and for the identification of agonisits and antagonists. These utilities are all non-specific because they are applicable to a broad class of molecules, namely proteins and nucleic acids. Any nucleic acid can be used to detect itself, and likewise, any polypeptide can be used to raise antibodies. Thus, these utilities are not sufficient to meet the standard under 101.

The specification asserts that the encoded proteins are useful in methods for regenerating damaged or severed peripheral nerves or in therapeutics (p. 4, lines 14-16 and lines 19-20). The specification teaches that members of the neural Ig-superfamily (of which the instantly disclosed molecules are postulated to be members) play critical roles in a variety of different aspects of neural development and function (p. 8, lines 17-35). The specification speculates that the DS-

CAM polypeptide may be responsible for holoprosencephaly and/or several phenotypes of Down Syndrome (p. 21, lines 15-30). The specification speculates that the DS-CAM molecule can be used to diagnose a variety of diseases, including mental retardation, holoprosencephaly, agenesis of the corpus callosum, or schizencephaly (p. 44, lines 17-30). However, the specification does not provide any evidence to support any of these utilities beyond the knowledge that this gene maps to the region of the genome that is associated with Down Syndrome and this gene is a putative cell adhesion molecule. Thus, none of these proposed utilities is considered to be a substantial utility because they are all speculative and would require further experimentation to reasonably confirm which, if any, are actual utilities of the instantly disclosed human and mouse molecules. These asserted utilities are an invitation for a researcher to further experiment to determine how to utilize the claimed nucleic acid molecules.

Claims 1 and 31-49 are also rejected under 35 U.S.C. 112, first paragraph. Specifically, since the claimed invention is not supported by either a specific and substantial asserted utility or a well established utility for the reasons set forth above, one skilled in the art clearly would not know how to use the claimed invention.

Applicant's remarks with regard to a previously set forth utility rejection are addressed herein (see papers 15 and17).

The previous rejection was for a lack of specific and did not address the issue that many of the asserted utilities, while they may be specific, are not substantial utilities because they would require further experimentation to reasonably confirm a real world utility. Applicant refers to an asserted utility of genetic testing and diagnosis of Down Syndrome on pates 43-45 of the specification. This section of the specification discusses the fact that the DS-CAM molecule

is located in a region of the genome that is associated with down syndrome in both mice and humans. It goes on to suggest that in light of this fact that a number of different conditions can be diagnosed. This is considered to be an assertion of a utility that is not substantial because no guidance or evidence is provided as to which of the list of conditions can in fact be diagnosed using the instant DS-CAM molecules. The instant utility rejection is not directed at the question of whether or not applicant has isolated an actual cDNA sequence, thus the remarks to this end are moot.

Claim Rejections - 35 USC § 112

15. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

16. Claims 33, 34, 35, 36, 37, and 49 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The limitation in these claims which requires that the encompassed nucleic acids hybridize to "substantially the entire complement" is indefinite because the metes and bounds of how much of the entire complement is required to be a "substantial" portion is not known. Neither the specification nor the claims provide any guidance in this matter, and thus, it is not clear what portion of the recited sections is required to be a "substantial" portion.

Claim Rejections - 35 USC § 102

17. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

18. Claims 33, 35, 36, 37, 44, 46, 47, and 49 are rejected under 35 U.S.C. 102(e) as being anticipated by McCarthy et al. (US 5952171).

McCarthy et al. teach an isolated nucleic acid comprising the nucleotide sequence of a complementary DNA that hybridizes under high stringency to substantially the entire complement of the nucleic acid encoding amino acids 1 to 1473 of instant SEQ ID NO: 11. Specifically, SEQ ID NO: 6 taught by McCarthy et al. comprises a sequence that has 74.57% similarity with a nucleic acid that encodes a portion of instant SEQ ID NO: 11, particularly amino acids 1-463 of SEQ ID NO: 11 (see alignment attached). This nucleic acid would hybridize under high stringency conditions to at substantially the entire complement, wherein in this case about one third of the complement is considered to be "substantially" the entire complement.

McCarthy et al. teach an isolated nucleic acid comprising the nucleotide sequence of a complementary DNA that hybridizes under high stringency to substantially the entire complement of the nucleic acid recited in instant SEQ ID NO: 7. Specifically, SEQ ID NO: 6 taught by McCarthy et al. comprises a sequence that has 65.1% identity nucleotides 76-840 of instant SEQ ID NO: 7, or substantially all of SEQ ID NO: 7 (see attached alignment).

McCarthy et al. teach oligonucleotide comprising at least 15 nucleotides of instant SEQ ID NO: 7 (see attached alignment of McCarthy's SEQ ID NO: 6 to instant SEQ ID NO: 7, which exemplify that SEQ ID NO: 6 taught by McCarthy et al. comprises several stretches of at least 15 nucleotides of SEQ ID NO: 7). The recitation of a "kit" in claim 46 is an intended use limitation that does not differentiate the nucleic acid taught by McCarthy et al. from the claimed invention.

McCarthy et al. teach vectors, host cells, and methods of expression using their SEQ ID NO: 6 which encodes their SEQ ID NO: 5 (Col. 3, 4, and 8, for example).

19. Claims 44 and 46 are rejected under 35 U.S.C. 102(e) as being anticipated by Baker et al. (US 5494818).

Baker et al. teach oligonucleotide comprising at least 15 nucleotides of the complement of instant SEQ ID NO: 8. Specifically, nucleotides 3155-3172 of SEQ ID NO: 1 taught by Baker et al. are the complement of nucleotides 98-115 of instant SEQ ID NO: 8. The recitation of a "kit" in claim 46 is an intended use limitation that does not differentiate the nucleic acid taught by Baker et al. from the claimed invention.

Conclusion

No claims are allowed. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Juliet C. Einsmann whose telephone number is (703) 306-5824. The examiner can normally be reached on Monday through Friday, from 9:00 AM until 4:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, W. Gary Jones can be reached on (703) 308-1152. The fax phone numbers for the

organization where this application or proceeding is assigned are (703) 308-4242 and (703) 305-3014.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

Juliet C. Einsmann
Examiner
Art Unit 1634

January 26, 2003

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Technology Center 1600

The top line is instant SEQ ID NO: 11, amino acids 1-463, the bottom line is SEQ ID NO: 6 from McCarthy et al.

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Qy       1 MetTrpIleLeuAla---LeuSerLeuPheGlnSerPheAlaAsnValPheSerGluAsp 19
           ||||||::::::      |||   |||      |||                   ||||||
Db      99 ATGTGGCTGGTAACTTTCCTCCTGCTCCTGGACTCTTTACACAAAGCCCGCCCTGAAGAT 158

Qy      20 LeuHisSerSerLeuTyrPheValAsnAlaSerLeuGlnGluValValPheAlaSerThr 39
           :::   :::||||||||||||||||||   |||||||||:::|||   |||:::|||:::
Db     159 GTTGGCACCAGCCTCTACTTTGTAAATGACTCCTTGCAGCAGGTGACCTTTTCCAGCTCC 218

Qy      40 ThrGlyThrLeuValProCysProAlaAlaGlyIleProProValThrLeuArgTrpTyr 59
              |||   :::||||||||||||||||||||||   |||         ||||||||||||
Db     219 GTGGGGGTGGTGGTGCCCTGCCCGGCCGCGGGCTCCCCCAGCGCGGCCCTTCGATGGTAC 278

Qy      60 LeuAlaThrGlyGluGluIleTyrAspValProGlyIleArgHisValHisProAsnGly 79
           ||||||||||||::::::|||||||||||||||   |||||||||||||||   ||||||
Db     279 CTGGCCACAGGGGACGACATCTACGACGTGCCGCACATCCGGCACGTCCACGCCAACGGG 338

Qy      80 ThrLeuGlnIlePheProPheProProSerSerPheSerThrLeuIleHisAspAsnThr 99
           |||||||||::::::||||||   ||||||:::|||::::::   ||||||||||||
Db     339 ACGCTGCAGCTCTACCCCTTCTCCCCCTCCGCCTTCAATAGCTTTATCCACGACAATGAC 398

Qy     100 TyrTyrCysThrAlaGluAsnProSerGlyLysIleArgSerGlnAspValHisIleLys 119
           |||:::|||||||||||||||   :::|||||||||||||||   ::::::   :::|||
Db     399 TACTTCTGCACCGCGGAGAACGCTGCCGGCAAGATCCGGAGCCCCAACATCCGCGTCAAA 458

Qy     120 AlaValLeuArgGluProTyrThrValArgValGluAspGlnLysThrMetArgGlyAsn 139
           ||||||   |||||||||||||||||||||||||||||||:::::::||||||||||||
Db     459 GCAGTTTTCAGGGAACCCTACACCGTCCGGGTGGAGGATCAAAGGTCAATGCGTGGCAAC 518

Qy     140 ValAlaValPheLysCysIleIleProSerSerValGluAlaTyrIleThrValValSer 159
           |||||||||||||||||:::|||||||||||||||:::   |||::::::|||||||||
Db     519 GTGGCCGTCTTCAAGTGCCTCATCCCCTCTTCAGTGCAGGAATATGTTAGCGTTGTATCT 578

Qy     160 TrpGluLysAspThrValSerLeuValSerGlySerArgPheLeuIleThrSerThrGly 179
           ||||||||||||||||||::::::      :::||||||   ||||||      |||
Db     579 TGGGAGAAAGACACAGTCTCCATCATCCCAGAAAACAGGTTTTTTATTACCTACCACGGC 638

Qy     180 AlaLeuTyrIleLysAspValGlnAsnGluAspGlyLeuTyrAsnTyrArgCysIleThr 199
              |||||||||   |||||||||   ||||||   |||      ||||||||||||||
Db     639 GGGCTGTACATCTCTGACGTACAGAAGGAGGACGCCCTCTCCACCTATCGCTGCATCACC 698

Qy     200 ArgHisArgTyrThrGlyGluThrArgGlnSerAsnSerAlaArgLeuPheValSerAsp 219
           :::|||:::|||:::||||||||||||||||||||   |||||||||   |||:::|||
Db     699 AAGCACAAGTATAGCGGGGAGACCCGGCAGAGCAATGGGGCACGCCTCTCTGTGACAGAC 758

Qy     220 ProAlaAsnSerAlaProSerIleLeuAspGlyPheAspHisArgLysAlaMetAlaGly 239
           ||||||   |||   |||:::|||||||||||||||      ::::::      ||||||
Db     759 CCTGCTGAGTCGATCCCCACCATCCTGGATGGCTTCCACTCCCAGGAAGTGTGGGCCGGC 818
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Qy    240 GlnArgValGluLeuProCysLysAlaLeuGlyHisProGluProAspTyrArgTrpLeu 259
          ||||||||||||||||   |||   |||:::|||   |||      |||||||||
Db    819 CACACCGTGGAGCTGCCCTGCACCGCCTCGGGCTACCCTATCCCCGCCATCCGCTGGCTC 878

Qy    260 LysAspAsnMetProLeuGluLeuSerGlyArgPheGlnLysThrValThrGlyLeuLeu 279
          ||||||      ||||||            |||:::   |||   :::|||||||||
Db    879 AAGGATGGCCGGCCCCTCCCGGCTGACAGCCGCTGGACCAAGCGCATCACAGGGCTGACC 938

Qy    280 IleGluAsnIleArgProSerAspSerGlySerTyrValCysGluValSerAsnArgTyr 299
          |||   ::::::|||      |||||||||:::|||:::|||||||||:::|||   :::
Db    939 ATCAGCGACTTGCGGACCGAGGACAGCGGCACCTACATTTGTGAGGTCACCAACACCTTC 998

Qy    300 GlyThrAlaLysValIleGlyArgLeuTyrValLysGlnProLeuLysAlaThrIleSer 319
          |||:::|||:::      |||   |||   |||      ||||||      |||::::::
Db    999 GGTTCGGCAGAGGCCACAGGCATCCTCATGGTCATTGATCCCCTTCATGTGACCCTGACA 1058

Qy    320 ProArgLysValLysSerSerValGlySerGlnValSerLeuSerCysSerValThrGly 339
          |||:::|||:::|||:::   :::||||||   |||   |||||||||::::::||||||
Db   1059 CCAAAGAAGCTGAAGACCGGCATTGGCAGCACGGTCATCCTCTCCTGTGCCCTGACGGGC 1118

Qy    340 ThrGluAspGlnGluLeuSerTrpTyrArgAsnGlyGluIleLeuAsnProGlyLysAsn 359
          :::   :::      :::   ||||||||||||   |||::::::   |||   :::
Db   1119 TCCCCAGAGTTCACCATCCGCTGGTATCGCAACACGGAGCTGGTGCTGCCTGACGAGGCC 1178

Qy    360 ValArgIleThrGlyIleAsnHisGluAsnLeuIleMetAspHisMetValLysSerAsp 379
          :::   |||   |||::::::::::|||   |||::::::            ||||||
Db   1179 ATCTCCATCCGTGGGCTCAGCAACGAGACGCTGCTCATCACCTCGGCCCAGAAGAGCCAT 1238

Qy    380 GlyGlyAlaTyrGlnCysPheValArgLysAspLysLeuSerAlaGlnAspTyrValGln 399
             ||||||||||||||||||      :::         :::||||||||||:::
Db   1239 TCCGGGGCCTACCAGTGCTTCGCTACCCGCAAGGCCCAGACCGCCCAGGACTTTGCCATC 1298

Qy    400 ValValLeuGluAspGlyThrProLysIleIleSerAlaPheSerGluLysValValSer 419
          :::   ||||||||||||||||||:::|||:::|||:::||||||||||||||||||:::
Db   1299 ATTGCACTTGAGGATGGCACGCCCCGCATCGTCTCGTCCTTCAGCGAGAAGGTGGTCAAC 1358

Qy    420 ProAlaGluProValSerLeuMetCysAsnValLysGlyThrProLeuProThrIleThr 439
          |||   |||      ||||||||||||      ||||||   |||   ||||||:::|||
Db   1359 CCCGGGGAGCAGTTCTCACTGATGTGTGCGGCCAAGGGCGCCCCGCCCCCCACGGTCACC 1418

Qy    440 TrpThrLeuAspAspAspProIleLeuLysGlyGlySerHisArgIleSerGlnMetIle 459
          |||   |||||||||:::||||||::::::   ||||||||||||   :::|||
Db   1419 TGGGCCCTCGACGATGAGCCCATCGTGCGGGATGGCAGCCACCGCACCAACCAGTACACC 1478

Qy    460 ThrSerGluGly 463
             |||:::|||
Db   1479 ATGTCGGACGGC 1490
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The top line is instant SEQ ID NO: 7, the bottom line is SEQ ID NO: 6 from McCarthy et al.

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Qy     76 CTCGCGGGAGGCCGGGCAGCAGCAGGGGCATGTGGATACTGGCTCTCTCCTTGTTCCAGA 135
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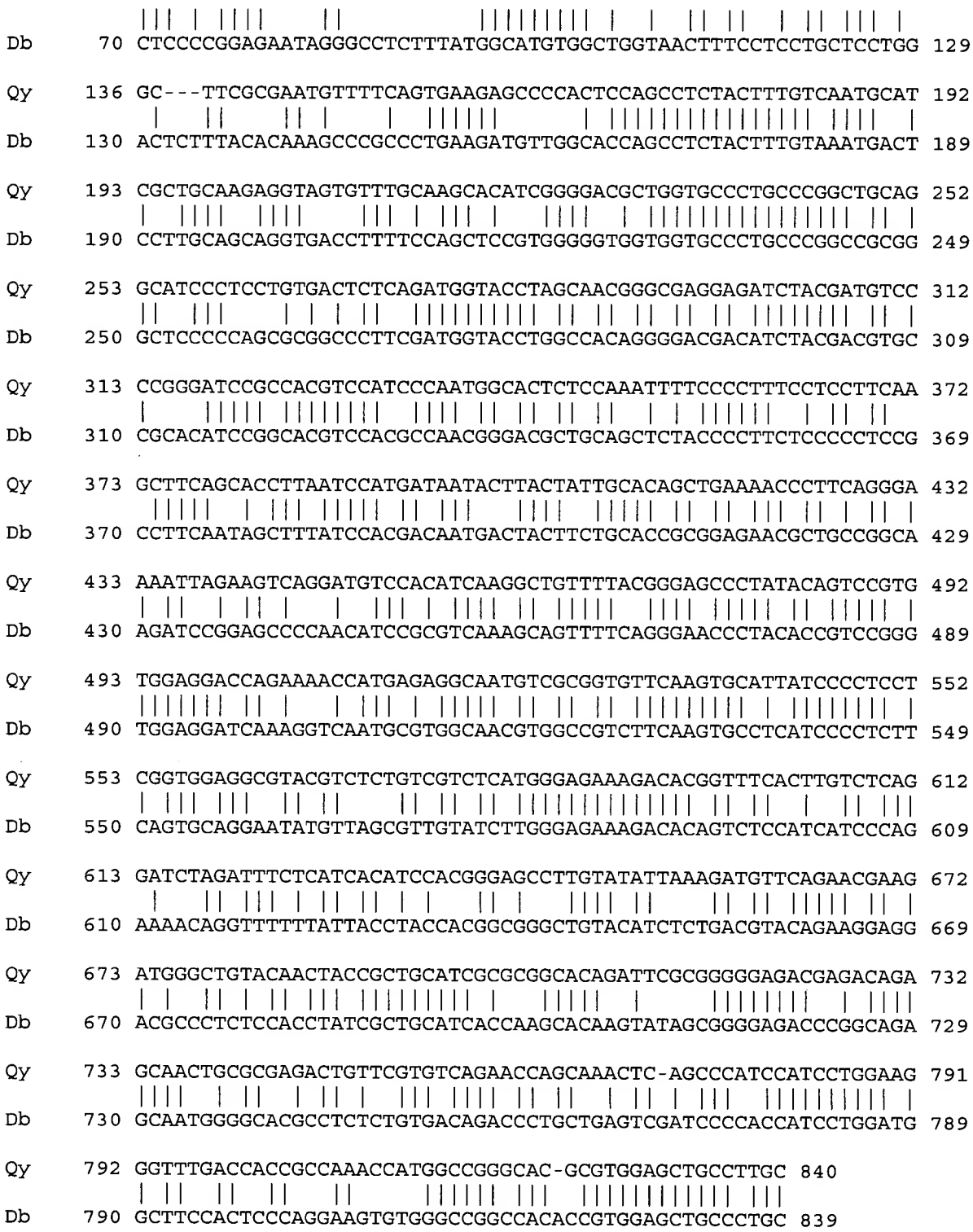
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Qy 136 GC---TTCGCGAATGTTTTCAGTGAAGAGCCCCACTCCAGCCTCTACTTTGTCAATGCAT 192
Db 130 ACTCTTTACACAAAGCCCGCCCTGAAGATGTTGGCACCAGCCTCTACTTTGTAAATGACT 189
Qy 193 CGCTGCAAGAGGTAGTGTTTGCAAGCACATCGGGGACGCTGGTGCCCTGCCCGGCTGCAG 252
Db 190 CCTTGCAGCAGGTGACCTTTTCCAGCTCCGTGGGGGTGGTGGTGCCCTGCCCGGCCGCGG 249
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Qy 313 CCGGGATCCGCCACGTCCATCCCAATGGCACTCTCCAAATTTTCCCCTTTCCTCCTTCAA 372
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Db 370 CCTTCAATAGCTTTATCCACGACAATGACTACTTCTGCACCGCGGAGAACGCTGCCGGCA 429
Qy 433 AAATTAGAAGTCAGGATGTCCACATCAAGGCTGTTTTACGGGAGCCCTATACAGTCCGTG 492
Db 430 AGATCCGGAGCCCCAACATCCGCGTCAAAGCAGTTTTCAGGGAACCCTACACCGTCCGGG 489
Qy 493 TGGAGGACCAGAAAACCATGAGAGGCAATGTCGCGGTGTTCAAGTGCATTATCCCCTCCT 552
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Qy 613 GATCTAGATTTCTCATCACATCCACGGGAGCCTTGTATATTAAAGATGTTCAGAACGAAG 672
Db 610 AAAACAGGTTTTTTATTACCTACCACGGCGGGCTGTACATCTCTGACGTACAGAAGGAGG 669
Qy 673 ATGGGCTGTACAACTACCGCTGCATCGCGCGGCACAGATTCGCGGGGGAGACGAGACAGA 732
Db 670 ACGCCCTCTCCACCTATCGCTGCATCACCAAGCACAAGTATAGCGGGGAGACCCGGCAGA 729
Qy 733 GCAACTGCGCGAGACTGTTCGTGTCAGAACCAGCAAACTC-AGCCCATCCATCCTGGAAG 791
Db 730 GCAATGGGGCACGCCTCTCTGTGACAGACCCTGCTGAGTCGATCCCCACCATCCTGGATG 789
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Db 790 GCTTCCACTCCCAGGAAGTGTGGGCCGGCCACACCGTGGAGCTGCCCTGC 839